Effects of COVID-19 on Respiratory System

Solunum Sistemi Üzerinde COVID-19'un Etkileri

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ABSTRACT

Coronavirus disease 2019 (COVID-19) was caused by a novel type of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was originated in Wuhan, China in December 2019. It spreads rapidly all over the world since respiratory virus infection can occur through many easy ways (*e.g.* contact, droplet spray, aerosol) and besides, asymptomatic people also have contagiousness. So far, there have been 23,491,520 confirmed cases of COVID-19, including 809,970 deaths, reported to World Health Organization (WHO), which declared it as a significant threat to global health. Fever, fatigue, and dry cough are the commonly observed symptoms in the patients. In COVID-19, the main affected system is respiratory system and some cases demonstrate a rapid progression to acute respiratory distress syndrome (ARDS), while other organs are less involved. Angiotensin-converting enzyme 2 receptor-virus association is essential and responsible for the development of the disease. SARS-CoV-2 causes deaths through its severe effects on the respiratory system.

Key Words; COVID-19, viral entry, ACE2 receptor, respiratory system, SARS-CoV, ARDS

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ÖZET

Coronavirus hastalığı 2019 (COVID-19) ağır akut solunum sendromu coronavirus 2 (SARS-CoV-2) nedeniyle oluşmaktadır. Wuhan'da (Çin) Aralık 2019'da ortaya çıkmıştır. Solunum yolunun viral enfeksiyonu kolay yolla bulaşması (temas, damlacık, aerosol) ve asemptomatik kişilerin bulaştırıcı olması nedeniyle dünya çapında hızla yayılmaktadır. Şimdiye kadar Dünya Sağlık Örgütü'ne (DSÖ) bildirilmiş 23,491,520 onaylanmış COVID-19 vakası, 809,970 ölüm (dahil) bulunmaktadırr ve DSÖ bunu küresel sağlığa yönelik önemli bir tehdit olarak bildirmiştir. Hastalarda ateş, yorgunluk, kuru öksürük yaygın olarak gözlenen semptomlardır. COVID-19'da esas etkilenen sistem solunum sistemidir ve bazı vakalar akut solunum sıkıntısı sendromuna (ARDS) hızla yönelmektedir, diğer organların etkilenmesi daha az gerçekleşmektedir. Anjiyotensin dönüştürücü enzim 2 reseptör ile virüs ilişkisi hastalığın ilerlemesinden sorumludur ve SARS-CoV-2 solunum sisteminde ciddi etkileri olmasından dolayı ölümlere neden olmaktadır.

Anahtar Sözcükler; COVID-19, viral giriş, ACE2 reseptör, solunum sistemi, SARS-CoV-2, ARDS

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INTRODUCTION

According to World Health Organization (WHO) viral diseases continue to emerge. These diseases are serious issues for public health. In the past two decades, several viral outbreaks have been recorded, such as severe acute respiratory syndrome coronavirus (SARS-CoV) (2002-2003), H1N1 influenza (2009), and the Middle East respiratory syndrome coronavirus (MERS-CoV) (2012, Saudi Arabia) (1). These serious cases are life-threatening diseases. They are transmitted *via* air and droplets and from infected subjects or infection carriers or the contaminated surfaces (2). The novel virus emerged in Wuhan, China in late 2019, which was called SARS-CoV-2 by the WHO. It spreads rapidly worldwide and has caused a pandemic. In the early cases, as causative agent could not be identified as they were diagnosed as pneumonia of unknown etiology (3). This virus is in the Coronaviridae family as be the other coronaviruses. Coronavirinae subfamily, where the coronaviruses are located, is divided into four subfamilies, i. alpha, ii. beta, iii. gamma and iv. delta. Coronavirus name comes from the word "crown" since the coronavirus appears as a crown under an electron microscope. Coronaviruses (CoVs) are enveloped, non-segmented, single-stranded, and positive-sense RNA viruses (4). SARS-CoV-2 (Severe Acute Respiratory Syndrome), belonging to beta subfamily genera, causes COVID-19 (5,6). SARS-CoV-2 is zoonotic, which was originated from animals such as horseshoe bats and then transmitted to humans (7). Figure 1 shows the structure of coronavirus.

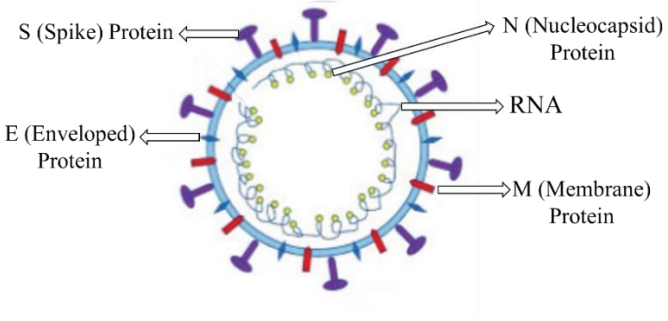

Figure 1. Structure of coronavirus

While the disease called COVID-19 (Coronavirus disease 2019) progresses with asymptomatic or mild findings in some people, approximately 20% of the cases have severe symptoms requiring hospitalization. The morbidity and mortality of COVID-19 are mostly associated with acute viral pneumonias and severe acute respiratory distress syndrome (ARDS) (8, 9).

Transmission of virus

When an infected person coughs or sneezes, the transmission of the disease takes place *via* droplets. Asymptomatic people also have contagiousness. In addition, it is transmitted due to contact of the droplets scattered as a result of coughing and sneezing of the patients, and then the hands are taken to the mouth, nose or eye mucosa (10).

Viral entry into the host cell

It is thought that the virus can enter the host cell using its angiotensin-converting enzyme-2 (ACE2) receptor. ACE2 is found in high levels in respiratory epithelium and alveolar type II cells. The virus is more sensitive in tissues, such as nasal mucosa, bronchi, and lung parenchyma, with high ACE-2 receptor levels. Therefore, the respiratory system is often affected by the virus. The inflammation mediated by macrophages and granulocytes in lung tissue is the main cause of respiratory disorders in the disease development (11). Spike protein plays an essential role in binding to receptors. Coronavirus ACE2 receptor binding occurs *via* the spike protein which has two subunits, S1 and S2. S1 mediates binding between coronavirus and receptor. S2 has trimeric structure that plays role in fusion with the infected cell. S1 is divided into 2 regions, S and N-terminal domains. These domains mediate binding to the various cellular receptors containing carbohydrates or proteins at the binding sites. SARS-CoV-2 binds to ACE2 receptor (12-14).

Phases of development of the disease

The SARS-CoV-2 virus infects body, where the body reacts on the 4 phases.
Phase 1: Cell invasion and viral replication in the nose
Phase 2: Replication in the lung and immune system alerted
Phase 3: Pneumonia
Phase 4: Acute respiratory distress syndrome, the cytokine storm, and multiple organ failure

General symptoms of the disease

After SARS-CoV-2 is frequently transmitted, viral replication occurs primarily in the mucosal epithelium of the upper respiratory tract, such as the nasopharynx. Then, replication often continues in the lower respiratory tract (15-17). The incubation period of this disease is 2-14 days, however, in most cases this period may take 4-5 days. It was stated that 80% of the patients had the disease with mild to moderate severity, 13.8% had severe illness and 6.1% had critically ill (respiratory failure, septic shock and/or multi-organ dysfunction or failure) (18). The most commonly observed symptoms are fever, fatigue, and dry cough. Besides these symptoms, headache, nasal congestion, runny or stuffy nose; sore throat, myalgia, and arthralgia may occur.

Also, white blood cell counts, lymphopenia, or thrombocytopenia, with the increased C-reactive protein level may be observed normal or lower in COVID-19 patients. (19). Mild or moderate cases of pneumonia are present or absent. In severe cases, dyspnea, respiratory frequency ≥ 30 / minute, blood oxygen saturation ≤ 93%, PaO_2 / FiO_2 ratio < 300 and / or more than 50% of the lung area of infiltrated areas are observed (20).

The effects of respiratory system

The first signs of the disease usually appear as dry cough and fever. After about 5-7 days, lung function is impaired and shortness of breath appears. Furthermore, people who have additional or chronic diseases such as asthma, heart disease, and chronic lung disease can develop shortness of breath earlier and usually feel a greater severity of gasping (21). Following inflammation in the lung, gas exchange is disrupted. This disrupts the oxygenation and causes hypoxemia. After this point, a rapid deterioration in respiratory functions may occur. Respiratory injury in 10-20% of severe patients can become ARDS (22). This condition can occur in 8^{th}-14^{th} days of the disease. Therefore, the first treatment approach should be oxygen therapy at the time of hypoxemia (oxygen saturation; SpO_2 < 93%). However, some patients may develop respiratory failure despite early oxygen therapy. The next step of therapy in these patients is non-invasive ventilation (NIV) or high-flow nasal oxygen therapy (HFNO). A rapid improvement in partial arterial oxygen pressure (PaO_2)/inspired oxygen fraction (FiO_2) is observed with the application of NIV or HFNO treatments. However, in some patients, clinical deterioration may continue and the patient may need invasive mechanical ventilation (5,23). The development of the SARS-CoV-2 infection on the respiratory system is presented in Figure-2.

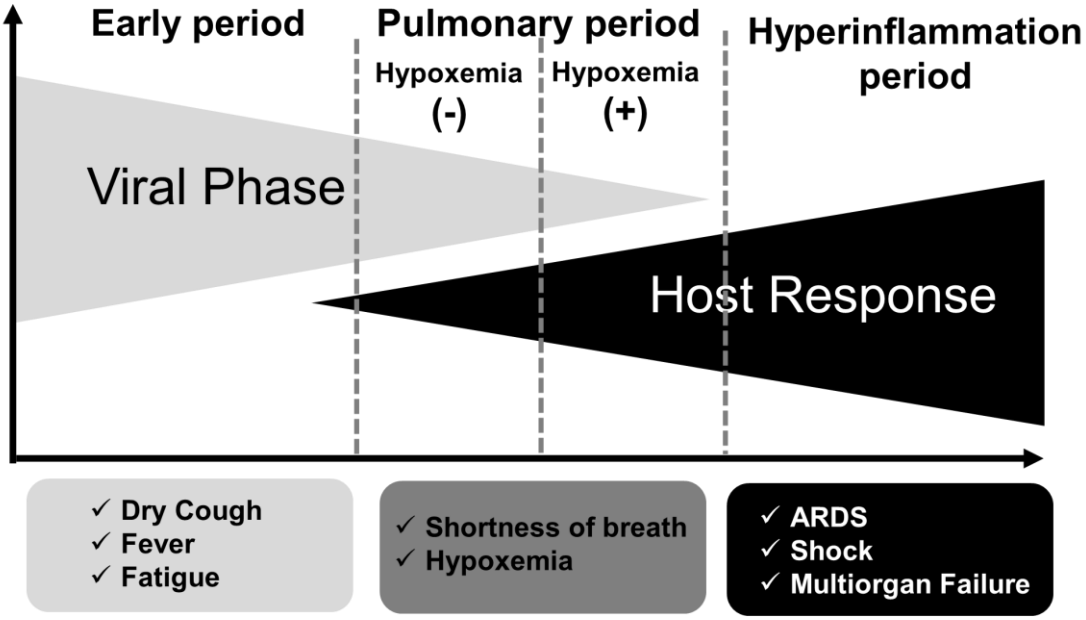

Figure 2. The development of the SARS-CoV-2 infection on the respiratory system

In some cases, studies revealed that the symptoms of severe pneumonia, fever, and dry cough are experienced at the beginning of the disease. Symptoms of upper respiratory tract symptoms such as rhinorrhea, sneezing, and sore throat are seen in very few patients. This indicates that lower respiratory tract infection is more likely in the patients (24).

Data from the cases reflect ground-glass opacities in both lung parenchyma and consolidated areas in the lung on chest computerized tomography (CT) scan findings. When the severity of the disease progresses to an intermediate level, in some cases widespread lung opacities and increased density are observed. In thoracic CT scans of intensive care patients, multiple lobular and subsegmental consolidated areas in both lungs are noticed (24). Findings in early phase of the disease include prominent alveolar edema in the lung lobe and reactive pneumocyte hyperplasia accompanied by inflammatory infiltration. Some of the type II alveolar epithelial cells have necrosis and desquamation (5, 25).

Some of the hospitalized patients develop cytokine release storms (CRSs) that lead fatal results (26). So far cytokine storm seems to be the most important event associated with COVID-19. Cytokine storm syndrome, a fulminant and fatal hypercytokinemia associated with multiorgan failure can be seen in some of the COVID-19 patients with severe conditions. Effects of various immune active molecules cause the cytokine storm and consequently occurring ARDS. Main components that take part in the occurrence of cytokine storm are chemokines, TNF-a, interleukins (IL), interferons, and colony stimulating factors. Among interleukins, some studies found that, in COVID-19 patients, serum levels of IL-6 are seen to be increased and a positive relation between disease severity and its level in circulation is shown (27). Currently, while using well-known mechanism of CRS treatments have focused on and directed to the strategy of preventing CRS and all possible cytokines have being addressed. All possible cytokines are investigated by researchers to find something to treat COVID-19 infection.

CONCLUSION

The SARS-CoV-2 outbreak remains critical. High quality health care should be applied and individual protection methods (mask, at least 1-1.5 m distance, residential) should be applied carefully due to the rapid spread of the virus. Recent techniques such as high-flow nasal cannula (HFNC) oxygen therapy application provide an efficient therapy by delivering a high flow of heated and humidified gas, and also good alternative treatment for hypoxemic acute respiratory failure.

Conflict of Interest
The authors declare that there is no conflict of interest.

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